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EXAMINER	
HINES, JANA A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/937,066	ALPAR ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,11-17,20-22,37 and 44-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,11-17,20-22,37 and 44-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Prosecution Application

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2009 has been entered.

Amendment Entry

2. The amendment filed February 13, 2009 has been entered. Claim 15, 20 and 22 have been amended. Claims 2-4, 7-10, 18-19, 23-36 and 38-43 are cancelled. Claims 44-71 are newly added. Claims 1, 5-6, 11-17, 20-22 and 37 are under consideration in this office action.

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Ruprecht et al., (WO 92/05791); and

b) The rejection of Claims 1, 5-6, 11-15 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncan et al., in view of Ruprecht et al.

Response to Arguments

4. Applicant's arguments filed February 13, 2009 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1, 5-6, 11-15, 20, 44-48, 51, 62, 65-68 and 71 are rejected under 35 U.S.C. 102(a) as being anticipated by Amsden et al., (WO 99/57176).

The claims are drawn to a pharmaceutical composition comprising a biologically active agent that is capable of generating a protective immune response in an animal and an immunostimulant amount of N-carboxymethyl chitosan or a salt thereof. The claims are drawn to a pharmaceutical composition comprising particles comprising a first material, N-carboxymethyl chitosan or a salt thereof and a biologically active agent capable of generating a protective immune response in an animal or a human when administered to the animal or the human, wherein the ratio of the first material to the N-carboxymethyl chitosan or the salt thereof is from 99:1 to 9:1 w/w. And the claims are drawn to a pharmaceutical composition comprising an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof and particles comprising a first material and a biologically active agent capable of generating a protective immune response in an animal or a human.

Amsden et al., teach the application of microspheres composed of biodegradable, biocompatible polymer and contains a bioactive agent dispersed therein (page 23, lines 3-6). Amsden et al., teach delivering a bioactive agent to a subject in need of treatment (page 23, lines 15-16). Examples of suitable bioactive agents include anti-proliferative agents, steroids, analgesics, narcotic antagonists, antibiotics, anti-fungals, anti-histamines, anti-asthmatics, B-blockers and anti-cancer agents (page 23, lines 18-23). Amsden et al., teach therapeutic microspheres comprising a bioactive agent being a pharmacologically active peptide, antigen, or antibody explemplifed by a microsphere that bears an infectious agent antigen for vaccination (page 24, lines 1-3). Amsden et al., teach the composition formed into microspheres composed of hydrophilic polymers selected from polysaccharides such as chitosan, N,O-carbomethyl chitosan, O-carboxymethyl chitosan, N-carboxymethyl chitosan, blends, copolymers and combinations of these polymers (page 9, lines 12-26). Amsden et al., teach the first composition being poly(lactide) and a second composition being co-glycolide or poly(glycolide) at a ratio of 85:15 , see Example 1 at page 26. Amsden et al., teach microspheres incorporated into a second polymer, which are uniformly sized microspheres dispersed throughout a gel or viscous solution or dispersed throughout a solid biodegradable polymer scaffold (page 24, lines 7-10). Amsden et al., teach that It is noted that the polycationic carbohydrates capable of forming particles from 99:1 to 9:1 w/w include chitin derivatives, chitosans, cationic polypeptides, polyamino acids; which are all disclosed by Amsden et al. Amsden et al., teach polymers formed into microspheres composed of poly(lactide-co-glycolide) (PGLA) and other lipophilic

polymers such as polyesters including but not limited to poly-(L-lactide), poly(lactide) as well as protein or polypeptide such as poly(amino acids). It is noted that is a polymeric material has a molecular weight of 100 kDa or more.

Therefore Amsden et al., teach the invention as claimed.

Response to Arguments

6. Applicant's arguments filed February 13, 2009 have been fully considered but they are not persuasive.

The rejection of claims 1, 5-6, 11-15, 20, 44-48, 51, 62, 65-68 and 71 under 35 U.S.C. 102(a) as being anticipated by Amsden et al., is maintained.

Applicants argue that Amsden et al., fails to teach microspheres that comprise an immunostimulating amount of N-carboxymethyl chitosan or salt thereof. In response to applicant's argument that the Amsden et al., reference fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., an amount of N-carboxymethyl chitosan or salt thereof are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, because no specific amount is recited, thus amounts taught by Amsden et al, meet the limitations of the claims. Furthermore, Amsden et al., teach the composition formed into microspheres composed of N,O-carbomethyl chitosan, N-carboxymethyl chitosan, and combinations of polymers. Amsden et al., teach the first and a second polymers along with microspheres having a

second polymer within the first. Applicants arguments are not found persuasive and Amsden et al., meet the claim limitations therefore the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 5-6, 11-17, 20-22, 37, 44-51, 62, and 65-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eyles (1998. Vaccine. Vol.16(7):698-707) in view of Amsden et al., (WO 99/57176).

The claims are drawn to a pharmaceutical composition comprising a biologically active agent that is capable of generating a protective immune response in an animal and an immunostimulant amount of N-carboxymethyl chitosan or a salt thereof. The claims are drawn to a pharmaceutical composition comprising particles comprising a first material, N-carboxymethyl chitosan or a salt thereof and a biologically active agent capable of generating a protective immune response in an animal or a human when administered to the animal or the human, wherein the ratio of the first material to the N-carboxymethyl chitosan or the salt thereof is from 99:1 to 9:1 w/w. And the claims are drawn to a pharmaceutical composition comprising an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof and particles comprising a first

material and a biologically active agent capable of generating a protective immune response in an animal or a human.

Eyles et al., teach a pharmaceutical composition comprising poly-(L-lactide) microspheres co-encapsulated with *Yersinia pestis* V and F1 subunits that confer protection from pneumonic plague in mice (page 699, col.2). Eyles et al., teach that the F1 antigen confers resistance to phagocytosis and both F1 and V antigens are protective, although there is an additive effect in the combination (page 698, col.2). It is noted that the F1 peptide subunit is a glycoprotein. The commercially purchased poly-(L-lactide) has a molecular weight of 100 kDa and was used in a modified double emulsion solvent evaporation method (page 699, col.2). Eyles et al., teach effective vaccination requires affecting or utilizing musocal surfaces as portals of entry (page 698-699, col.2-1). Furthermore Eyles et al., teach that mucosal vaccination advantageously offers some degree of the induction of systemic immunity in concert with local responses due to translocation of antigenic material (page 699, col.1). Eyles teach that simple mucosal applications are ineffective because of enzymatic or chemical destruction, combined with poor absorption; therefore encapsulation of antigenic material within microparticulate polymeric carriers such as poly-DL-lactide protect the vaccines from degradation and enhance mucosal and systemic absorption (page 699, col.1). However Eyles et al., do not teach pharmaceutical compositions comprising N-carboxymethyl chitosan.

Amsden et al., has been discussed above as teaching compositions of microspheres having N-carboxymethyl chitosan, polymers and a bioactive agent dispersed therein.

Therefore it would have been prima facie obvious at the time of applicants' invention to modify the pharmaceutical composition comprising a biologically active agent as taught by Eyles et al., wherein the modification incorporates the use of N-carboxymethyl chitosan as taught by Amsden et al., in order to provide biodegradable, biocompatible polymers containing a bioactive agent dispersed therein in order to deliver a bioactive agent to a subject in need of treatment. No more than routine would have been required to modify the composition of Eyles et al., by incorporating N-carboxymethyl chitosan, because Amsden et al., teach it is well known to provide suitable bioactive agents including pharmacologically active antigen within therapeutic microspheres while Eyles teach et al., that the F1 antigen is both a peptide drug and a glycoprotein used within microsphere compositions. Furthermore, the limitations drawn to the ratios of particles to the polycationic carbohydrate are viewed as merely optimizing the experimental parameters and not imparting patentability; thus no more than routine skill would have been required to change the concentration in the well known compositions as taught by Eyles et al., in view of Amsden et al.

Response to Arguments

8. Applicant's arguments filed February 13, 2009 have been fully considered but they are not persuasive.

The rejection of claims 1, 5-6, 11-17, 20-22, 37, 44-51, 62, and 65-71 under 35 U.S.C. 103(a) as being unpatentable over Eyles (1998. Vaccine. Vol.16(7):698-707) in view of Amsden et al., (WO 99/57176) is maintained.

Applicants argue that Eyles fails to teach or suggest adding an immunostimulating amount of N-carboxymethyl chitosan to improve immunogenicity of the encapsulated plague vaccine. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that Amsden fails to teach or suggest that immunogenicity of vaccines can be improved by adding an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof. It is noted that there is not requirement that Amsden need to suggest or provide reasoning for improving immunogenicity of vaccines. “[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court stated that “just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.” There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the

subject matter is in fact inherent and disclosed in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.,* 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003). Therefore, Amsden et al., do not need to provide reasons why N-carboxymethyl chitosan or a salt thereof was included, because Amsden et al., clearly teach the inclusion of N-carboxymethyl chitosan or a salt thereof.

Applicants assert that, prior to the applicants' invention of the claimed pharmaceutical compositions, it would not have been obvious one of ordinary skill in the art to select N-carboxymethyl chitosan from the list of polymers suitable for microsphere production taught in Amsden, determine its immunostimulating amount, and combine such an amount with the plague vaccine disclosed in Eyles, in order to arrive at the pending claims. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Contrary to applicants assertion, one of ordinary skill in the art would have been motivated to modify the microparticle compositions as taught by Eyles et al., because Eyles et al., teach that effective compositions capable of generating a protective immune response require utilizing musocal surfaces as portals of entry; thus one of ordinary skill in the art would have a reasonable expectation of success in providing microparticle compositions with

significantly increased and beneficial mucosal absorption abilities without the disadvantage of enzymatic or chemical destruction, or poor absorption. And in this case, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by well known methods with no change in their respective functions, and the combination would have yielded predictable results at the time of the invention.

Claim Rejections - 35 USC § 103

9. Claims 1, 5-6, 11-17, 20-22, 37, 44-51, 62, and 65-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 97/20576 published June, 1997) in view of in view of Amsden et al., (WO 99/57176).

Illum teaches vaccine compositions comprising one or more biologically active agents capable of generating a protective immune response in an animal, an effective adjuvant and the polycationic carbohydrate, chitosan (page 1, lines 1-6). Illum teaches suitable antigens include tetanus toxoid and diphtheria toxoid (pages 4-5, lines 23-1). Illum teaches the pharmaceutical compositions are formulated in the form of microspheres (page 6, lines 22-24). Illum teaches that chitosans are known as mucosal absorption enhancers and upon administration, chitosan enhances the immune response of antigens and provides an enhanced effect upon the host (page 3, lines 1-6). However Illum does not teach pharmaceutical compositions comprising N-carboxymethyl chitosan or a salt thereof.

Amsden et al., has been discussed above as teaching compositions of microspheres having N-carboxymethyl chitosan, polymers and a bioactive agent dispersed therein.

Therefore it would have been prima facie obvious at the time of applicants' invention to modify the pharmaceutical composition comprising a biologically active agent as taught by Illum, wherein the modification incorporates the use of N-carboxymethyl chitosan as taught by Amsden et al., in order to provide biodegradable, biocompatible polymers containing a bioactive agent dispersed therein in order to deliver a bioactive agent to a subject in need of treatment. One of ordinary skill in the art would be motivated to modify the compositions as taught by Illum, because Illum teach the need for chitosans, which are well known mucosal absorption enhancers that also enhance the immune response of antigens; thereby providing a reasonable expectation

of success. Thus one of ordinary skill in the art would have a reasonable expectation of success in providing compositions having incorporating N-carboxymethyl chitosan, because Amsden et al., teach it is well known to provide suitable bioactive agents including pharmacologically active antigen within therapeutic microspheres. Finally it would have been advantageous to incorporate the N-carboxymethyl chitosan in the pharmaceutical composition, in order to achieve an enhanced effect upon the host.

Response to Arguments

10. Applicant's arguments have been fully considered but they are not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, one of ordinary skill in the art would be motivated to modify the compositions as taught by Illum, because Illum teach the need for chitosans, which are well known mucosal absorption enhancers that also enhance the immune response of antigens; and Amsden et al., teach the inclusion of N-carboxymethyl chitosan, thereby providing a reasonable expectation of success. Moreover, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by well known methods with no change in their respective functions, and the combination would have yielded predictable results at the time of the invention.

New Grounds of Objection Necessitated By Amendment

Claim Objections

11. Claims 44-71 are objected to because of the following informalities:

a) Claims 44, 52, and 62 recite a first material, however the claims fail to define what the first material is. Thus the metes and bounds of the claim are unclear and appropriate clarification is required to overcome the objection.

b) Claims 63-64 recite at least a part of the immunostimulating amount of N-carboxymethyl chitosan or a salt thereof are at the surface of the particle. However it is unclear exactly what part of the N-carboxymethyl chitosan or a salt thereof is at the surface. Appropriate correction is required.

New Grounds of Rejection Necessitated By Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 5-6, 11-15 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncan et al., (WO 94/20070 published September 1994) in view of Amsden et al., (WO 99/57176).

Duncan et al., teach compositions comprising: i) biologically active agents, such as immunogens or antigens at pages 4-5 para.1, ii) an adjuvant chemical having

adjuvant properties wherein the adjuvants include Pluronic™ block copolymers also known as cationic pluronics and polyamino acids such as polyarnithine at pages 9-10, para. 1; and iii) an acceptable carrier such as a mucoadhesive at page 6, para.1. Duncan et al., further teach that an enhancement in the immune response is observed when the adjuvant is combined with the immunogen and mucoadhesive (pages 10-11, para.2). The antigens are more immunogenic when they are incorporated into the polymeric microparticles, nanoparticles or liposomes (page 2, para.4). However Duncan et al., do not teach pharmaceutical compositions comprising N-carboxymethyl chitosan.

Amsden et al., has been discussed above as teaching compositions comprising providing an active agent and N-carboxymethyl-chitosan.

Therefore, it would have been prima facie obvious at the time of applicants' invention to have used the known N-carboxymethyl chitosan as taught by Amsden et al., and modify the compositions to include the biologically active antigen and agents capable of generating a protective immune response and providing the compositions in a microparticle formulation as taught by Duncan et al., in order to enhance the muchoadhesive properties. One of ordinary skill in the art would have a reasonable expectation of success by modifying the pharmaceutical compositions as taught by Duncan et a., because Duncan et al., teach the need for mucoadhesive which provide further enhancement in the immune response. Thus one of ordinary skill in the art would have a reasonable expectation of success in providing compositions having N-carboxymethyl-chitosan since Amsden et al., teach it is well known to provide pharmaceutical compositions comprising N-carboxymethyl-chitosan are effective in

patients. No more than routine would have been required to modify the composition of Duncan et al., to instead incorporate the N-carboxymethyl-chitosan into the pharmaceutical composition of Duncan which already comprises a mucoadhesive combined with biological active antigens and cationic pluronic in microparticle formation to achieve enhanced mucosal absorption. Finally it would have been advantageous to incorporate N-carboxymethyl-chitosan in the pharmaceutical composition, in order to achieve an enhanced effect upon the host.

Claim Rejections - 35 USC § 103

13. Claim 52-61, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (WO 97/20576 7) or Eyles (1998. Vaccine. Vol.16(7):698-707) and Amsden et al., (WO 99/57176) as applied to claim 62 above, and further in view of Cleary et al., (WO 96/21432 published July 18, 1996).

Both Illum or Eyles and Amsden et al., have been discussed above as teaching pharmaceutical compositions comprising particles comprising a first material and a biologically active agent capable of generating a protective immune response in an animal or human and N-carboxymethyl chitosan or a salt thereof. However none specifically recite the N-carboxymethyl chitosan or a salt thereof being at the surface of the particles.

Clearly et al., teach sustained and controlled local and systemic release of active agents to adhere to mucosal surfaces (page 3, lines 9-12). Cleary et al., teach the active agents have therapeutic effects either locally, upon the mucosal tissues and

underlying tissues or systemically delivered (page 3-4, lines 26-2). Cleary et al., teach mucoadhesive particles having a polymer which is mucoadhesive itself in particulate form (page 4-5, lines 26-1). Clearly et al., teach the particles as being microspheres, microparticles or microcapsules (page 5, lines 5-6). Cleary et al., teach coating the active substance with a bioerodible mucoadhesive polymer layer (page 7, line 1). Cleary et al., teach a particle having a drug containing core and a mucoadhesive coating made of a polymer that dissolves slowing resulting in retention of the active substance on the mucosal surface for an extended period of time (page 7, lines 5-15).

Therefore it would have been prima facie obvious at the time of applicants' invention to modify the pharmaceutical composition comprising a biologically active agent as taught by Illum or Eyles and Amsden et al., , wherein the modification incorporates the having the mucoadhesive N-carboxymethyl chitosan at the surface of the particle as taught by Cleary et al., in order to provide sustained and controlled local and systemic release of active agents to mucosal surfaces. One of ordinary skill in the art would be motivated to modify the compositions as taught by Illum/Eyles and Amsden et al., because Illum/Eyles and Amsden et al.., teach the need the mucoadhesive N-carboxymethyl chitosan are well known mucosal absorption enhancers that also enhance the immune response of antigens; thereby providing a reasonable expectation of success to have the mucoadhesive at the surface of the particle. Thus one of ordinary skill in the art would have a reasonable expectation of success in providing compositions having incorporating N-carboxymethyl chitosan at the surface of the particle because the art teach coating the active agent with a bioerodible mucoadhesive

polymer layer to allow the therapeutic active agents to be delivered either locally or systemically.

Conclusion

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645
/Mark Navarro/
Primary Examiner, Art Unit 1645